UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

ABBOTT GMBH & CO., KG; ABBOTT BIORESEARCH CENTER, INC.; and ABBOTT BIOTECHNOLOGY LTD.,	)	
Plaintiffs,	)	**Civil Action No. 09-11340-FDS**
v.	)	
CENTOCOR ORTHO BIOTECH, INC., and CENTOCOR BIOLOGICS, INC.	)	
Defendants.	)	

SECOND AMENDED MEMORANDUM AND ORDER ON CLAIM CONSTRUCTION

SAYLOR, J.

This is a patent dispute involving a pharmaceutical product.[1] Plaintiffs Abbott GmbH & Co., KG; Abbott Bioresearch Center, Inc.; and Abbott Biotechnology Ltd. (collectively "Abbott") seek a judgment that the drug Stelara, manufactured by defendants Centocor Ortho Biotech, Inc., and Centocor Biologics, Inc. (collectively "Centocor"), infringes upon its patents. Centocor seeks declarations of non-infringement and invalidity of Abbott's patents and seeks review of a decision of the Patent and Trademark Office's ("PTO") Board of Patent Appeals and Interferences.

The parties' allegations hinge on the construction of the claims in Abbott's U.S. Patent No. 6,914,128 (the "'128 patent") and its U.S. Patent No. 7,504,485 (the "'485 patent"). The Court conducted a *Markman* hearing with respect to the construction of the relevant claims on

[1] The Court issued its original claim construction order on March 15, 2011. That order was previously amended to correct an error in the text. This second amended order construes an additional term added to the claim construction at a later point in the proceedings, as set forth below.

November 9, 2010.

Abbott and Centocor dispute seven terms: (1) "neutralizing antibody;" (2) "neutralizes;" (3) "inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay;" (4) "inhibits human IFNγ production;" (5) "inhibits IL-12 binding to its receptor in an IL-12 receptor binding assay (RBA);" (6) "additional agent;" and (7) "human antibody."

I. Background

Abbott filed the application that ultimately produced the '128 and '485 patents on March 25, 1999.[2] The patents were issued on July 5, 2005, and March 17, 2009, respectively. They share the same specification (including description and drawings) but make different claims.

The Abbott patents are directed to antibodies that attach to a naturally-occurring protein in the human body called interleukin-12 ("IL-12"). IL-12 is part of a family of proteins called cytokines. These molecules communicate with cells in the immune system by binding to certain receptors on the surfaces of those cells. Structurally, IL-12 is composed of two smaller molecules called the p35 subunit and the p40 subunit.[3]

IL-12 is involved in the human immune system's inflammation response to infection. Overproduction of IL-12 can lead to a malfunctioning immune system that attacks the body's cells and tissues. This can cause auto-immune diseases such as psoriasis, where the body's immune system chronically targets healthy human tissue instead of foreign contaminants.

One way of treating such diseases is by inhibiting or blocking the effects of IL-12 through

[2] The application for the '485 patent was filed several years later as a divisional of the original application.

[3] The p40 subunit of IL-12 appears in at least one other molecule, called IL-23. That molecule comprises a p40 and a p19 subunit.

the use of antibodies. Antibodies are proteins that attach themselves to a target molecule—called an "antigen" for that antibody—by binding with a portion of that molecule called an "epitope." Antibodies being designed for treatment can have a number of desirable characteristics. One such characteristic is called "specificity." An antibody is highly specific to an antigen if it only attaches to that antigen. An antibody with low specificity can be less effective because some of the antibody attaches to other molecules, reducing the amount available to neutralize the target antigen and potentially causing unwanted side effects.

Two other desirable characteristics are called "affinity" and "neutralizing" ability. "Affinity" is the strength of an antibody's attachment to a target antigen.[4] "Neutralizing" ability is the capability of that antibody to prevent the target antigen from interacting with its environment. Although high affinity is commonly associated with neutralizing ability, an antibody may have high affinity but be non-neutralizing.

Affinity may be assessed using several kinds of "assays," or tests. One measure of effectiveness used during these tests is the concentration of an antibody required to cut the biological activity of the antigen in half. This number is known as the "IC_{50}" for that antibody.

In the case of IL-12, Abbott used three types of assays to assess the effectiveness of its antibodies: receptor-binding assays ("RBAs"), proliferation assays, and induction assays. In all three assays, it used a modified human blood cell called a phytohemagglutinin blast, or "PHA" blast.

In RBAs, Abbott used the knowledge that IL-12 binds to receptors on PHA blasts to test

[4] The '128 and '485 patents use the variable "K_d" to represent an antibody's affinity. This is the rate at which antibodies detach from the target molecule ("K_{off}") divided by the rate at which they attach to that molecule ("K_{on}"). Mathematically, this may be represented as $K_d = K_{off} / K_{on}$.

the ability of an antibody to prevent IL-12 from binding to those receptors. Researchers measured the amount of such binding in the presence and absence of the antibody to determine the IC_{50} for that antibody. Similarly, in proliferation assays, Abbott used the knowledge that IL-12 stimulates proliferation of PHA blasts to measure the amount of proliferation in the presence and absence of the IL-12 antibody. Finally, in induction assays, Abbott used the knowledge that IL-12 stimulates PHA blasts to produce a molecule called interferon-gamma ("IFNγ") to measure the amount of IFNγ produced in the presence and absence of the IL-12 antibody.

The Abbott patents each describe and claim antibodies that bind to an epitope located on the p40 subunit of IL-12. These antibodies are "recombinant," meaning that they were created using techniques to splice and recombine DNA. By binding to IL-12, these antibodies can prevent IL-12 from interacting with cells and causing a harmful auto-immune response. Abbott currently has an antibody product called "ABT-874" that treats psoriasis using this approach. The allegedly infringing drug Stelara, developed by Centocor, is another recombinant antibody product that treats psoriasis by binding to IL-12. ABT-874 is in late-stage clinical trials, while Stelara has been approved for sale in the United States.

On December 12, 2007, the PTO Board of Patent Appeals and Interferences declared an interference between the '128 patent and Centocor's pending 10/912,994 patent application for Stelara. This proceeding was instituted to determine which group of inventors was the first to invent the overlapping subject matter, and to determine whether the '128 patent was unpatentable for obviousness under 35 U.S.C. § 103. On August 6, 2009, the PTO Board ruled for Abbott on these issues.

On August 10, 2009, Abbott filed suit against Centocor in the District Court for the

District of Massachusetts, alleging that the sale of Stelara infringed upon the ’128 and ‘485 patents. On August 28, 2009, Centocor instituted actions in the District Court for the District of Columbia challenging the PTO Board’s ruling pursuant to 35 U.S.C. § 146 and seeking declarations of non-infringement and invalidity of Abbott’s ’128 and ’485 patents.

On December 18, 2009, the District Court for the District of Columbia granted Abbott’s motion to transfer the proceedings there to this district. On January 6, 2010, this Court denied Centocor’s motion to transfer proceedings here to the District of Columbia. All actions were thereafter consolidated in this Court.

The Court issued its original claim construction order on March 15, 2011; it was amended to correct an error on March 17. On March 16, the Court granted Centocor’s request to interpret the term “human antibody” as part of the claim construction, prompting this second amended order.

II. Legal Framework

The construction of claim terms is a question of law. *Markman v. Westview Instruments*, 517 U.S. 370, 372 (1996) (“[T]he construction of a patent, including terms of art within its claim, is exclusively within the province of the court.”).

In *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005) (*en banc*), the Federal Circuit clarified the proper approach to claim construction and set forth principles for determining the hierarchy and weight of the definitional sources that give the patent its meaning. The guiding principle of construction is “the meaning that the term would have to a person of ordinary skill in the art in question at the time of . . . the effective filing date of the patent application.” *Id.* at 1313. Courts thus seek clarification of meaning in “the words of the claims themselves, the

remainder of the specification, the prosecution history, and extrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art." *Id.* at 1314 (quoting *Innova/Pure Water, Inc. v. Safari Water Filtration Sys.*, 381 F.3d 1111, 1116 (Fed. Cir. 2004)).

A. The Words of the Claims Themselves

The claim construction analysis normally begins with the claims themselves.[5] The claims of a patent "define the invention to which the patentee is entitled the right to exclude." *Id.* at 1312 (citing *Innova*, 381 F.3d at 1115).

In some instances, the arrangement of the disputed term in the claims is dispositive. "This court's cases provide numerous . . . examples in which the use of a term within the claim provides a firm basis for construing the term." *Id.* at 1314. For example, because claim terms are normally used consistently throughout the patent, the meaning of a term in one claim is likely the meaning of that same term in another. *Id.* In addition, "the presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim." *Id.* at 1315.

B. The Specification

"The claims, of course, do not stand alone." *Id.* at 1315. Rather, "they are part of a fully

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[5] In *Phillips*, the Federal Circuit discredited the practice of starting the claim construction analysis with broad definitions found in dictionaries and other extrinsic sources:

> [I]f the district court starts with the broad dictionary definition . . . and fails to fully appreciate how the specification implicitly limits that definition, the error will systematically cause the construction of the claim to be unduly expansive. The risk of systematic overbreadth is greatly reduced if the court instead focuses at the outset on how the patentee used the claim term in the claims, specification, and prosecution history, rather than starting with a broad definition and whittling it down.

Id. at 1321. Of course, if no special meaning is apparent after reviewing the intrinsic evidence, claim construction might then "involve[] little more than the application of the widely accepted meaning of commonly understood words." *Id.* at 1314.

integrated written instrument, consisting principally of a specification that concludes with the claims." *Id.* (internal citations and quotations omitted). For that reason, the specification must always be consulted to determine a claim's intended meaning. "[T]he specification is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." *Id.* (citing *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)).

"In general, the scope and outer boundary of claims is set by the patentee's description of his invention." *On Demand Mach. Corp. v. Ingram Indus.*, 442 F.3d 1331, 1338 (Fed. Cir. 2006); *see also Phillips*, 415 F.3d at 1315-1317 ("[T]he interpretation to be given a term can only be determined and confirmed with a full understanding of what the inventors actually invented and intended to envelop with the claim"). "[T]he specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess." *Phillips*, 415 F.3d at 1316. It may also reveal "an intentional disclaimer, or disavowal, of claim scope by the inventor." *Id.* Therefore, the claims are to be construed in a way that makes them consistent with, and no broader than, the invention disclosed in the specification. *On Demand*, 442 F.3d at 1340 ("[C]laims cannot be of broader scope than the invention that is set forth in the specification."); *Phillips*, 415 F.3d at 1316 ("[C]laims must be construed so as to be consistent with the specification, of which they are a part.").

Nevertheless, courts must be careful to "us[e] the specification [only] to interpret the meaning of a claim" and not to "import[] limitations from the specification into the claim." *Phillips*, 415 F.3d at 1323; *see also Gillette Co. v. Energizer Holdings, Inc.*, 405 F.3d 1367, 1375 (Fed. Cir. 2005) (internal quotations omitted). A patent's "claims, not specification

embodiments, define the scope of patent protection." *Kara Tech. Inc. v. Stamps.com Inc.*, 582 F.3d 1341, 1348 (Fed. Cir. 2009); *see also Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1381 (Fed. Cir. 2009) ("[E]mbodiments appearing in the written description will not be used to limit claim language that has broader effect."). "In particular, we have expressly rejected the contention that if a patent describes only a single embodiment, the claims of the patent must be construed as being limited to that embodiment." *Phillips*, 415 F.3d at 1323. This is "because persons of ordinary skill in the art rarely would confine their definitions of terms to the exact representations depicted in the embodiments." *Id.*

Although this distinction "can be a difficult one to apply in practice[,] . . . . the line between construing terms and importing limitations can be discerned with reasonable certainty and predictability if the court's focus remains on understanding how a person of ordinary skill in the art would understand the claim terms." *Id.* Ultimately, "[t]he construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction." *Id.* at 1316 (citing *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998).

C. The Prosecution History

After the specification and the claims themselves, the prosecution history is the next best indicator of term meaning. The prosecution history consists of the complete record of the proceedings before the PTO and includes the prior art cited during the examination of the patent. *Id.* at 1317. "Like the specification, the prosecution history provides evidence of how the PTO and the inventor understood the patent." *Id.* "[T]he prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and

whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." *Id.* (citing *Vitronics*, 90 F.3d at 1582-83).

However, "because the prosecution history represents an ongoing negotiation between the PTO and the applicant, rather than the final product of that negotiation, it often lacks the clarity of the specification and thus is less useful for claim construction purposes." *Id.* As a result, courts generally require that "a patent applicant [] clearly and unambiguously express surrender of subject matter" to disavow claim scope during prosecution. *Voda v. Cordis Corp.*, 536 F.3d 1311, 1321 (Fed. Cir. 2008) (quoting *Sorensen v. Int'l Trade Comm'n*, 427 F.3d 1375, 1378 (Fed. Cir. 2005)).

D. Extrinsic Sources

Extrinsic evidence consists of "all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." *Phillips*, 415 F.3d at 1317. It "can help educate the court regarding the field of the invention and can help the court determine what a person of ordinary skill in the art would understand claim terms to mean." *Id.* at 1319. However, extrinsic evidence suffers from a number of defects, including its independence from the patent, potential bias, and varying relevance. *Id.* at 1318-19. Such evidence is therefore "unlikely to result in a reliable interpretation of patent claim scope unless considered in the context of the intrinsic evidence," and courts may consider, or reject, such evidence at their discretion. *Id.* at 1319.

III. Analysis

At the outset, the Court notes that the parties have resolved several previously disputed terms on their own. The terms and their agreed-upon constructions are as follows:

CLAIM TERM	AGREED-UPON CONSTRUCTION
"K_d"	"the dissociation constant of a particular antibody-antigen interaction"
"K_{off}"	"the off rate constant for dissociation of an antibody from the antibody/antigen complex"
"surface plasmon resonance"	"an optical phenomenon that allows for the analysis of real-time biospecific interactions by detection of alterations in protein concentrations within a biosensor matrix"
"recombinant antibody"	"antibody that is prepared, expressed, created or isolated by recombinant means"
"pharmaceutically acceptable carrier"	"any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like that are physiologically compatible, including one or more of water, saline, sugars, alcohols, polyalcohols, wetting or emulsifying agents, preservatives or buffers"

Accordingly, the Court will adopt the parties' proposed constructions of these terms.

The remaining disputed terms may be broadly divided into five aspects of the Abbott patents. The Court will address each in turn.

A. Limiting the Claim Terms of the '128 patent to IL-12

First, the parties dispute whether various claims in the '128 patent should be limited to antibodies and processes involving IL-12. The proposed constructions of the disputed terms in the '128 patent are:

CLAIM TERM	ABBOTT'S PROPOSED CONSTRUCTION	CENTOCOR'S PROPOSED CONSTRUCTION
"neutralizing antibody" (claims 7-15, 29-40)	"an antibody whose binding to an antigen results in inhibition of a biological activity"	"an antibody whose binding **to human IL-12** results in inhibition of a biological activity **of human IL-12**"
"inhibits [PHA] blast proliferation in an in vitro PHA assay" (claims 8-12, 33-37, 55-57)	"inhibits the proliferation of stimulated human PHA blasts"	"inhibits the proliferation of human PHA blasts **stimulated by IL-12**"
"inhibits human IFNγ production" (claims 13-15, 38-40, 58-60)	plain meaning	"inhibits the production of human interferon-γ **stimulated by IL-12**"

(Gunther Decl. Exs. 8, 9; Def. Op. Br. at 9-10, 12) (emphasis added). The core disagreement over these terms is whether they should be interpreted as limited to IL-12.[6] Abbott contends that the claim language is sufficiently clear on its face, even where that language is not explicitly limited to processes or characteristics related to IL-12. Centocor contends that the specification teaches only how to make antibodies that bind to IL-12 and that the claim terms of the '128 patent should not be construed more broadly.

1. "Neutralizing Antibody"

Although the term "neutralizing antibody" appears in a number of claims of the '128 patent, its use in the chain of claims ending in claim 7 is typical:

> 1. An isolated human antibody, or antigen-binding portion thereof **that binds to human IL-12 and dissociates from human IL-12** with a K_d of $l \times l0^{-10}$ M or less and a k_{off} rate constant of $l \times l0^{-3} s^{-1}$ or less, as determined by surface plasmon resonance.

[6] The parties also dispute the addition of "PHA blasts" to the construction of "inhibits human IFNγ production." This aspect of the dispute is discussed in a following section.

2. The isolated human antibody of claim 1 . . . .

3. The isolated human antibody of claim 1 . . . .

7. The isolated human antibody of any one of claims 1 to 3, wherein the antibody is a **neutralizing antibody**.

U.S. Patent No. 6,914,128 at col. 385 ll. 11-35 (filed Mar. 25, 1999) (emphasis added).

Centocor contends that the claims, as written, are unduly expansive. Because the "neutralizing" activity is not clearly limited to IL-12, the claims could cover an antibody "that inhibits *any* biological activity of *any* cytokine," which would be overbroad. (Def. Reply Br. at 5). In support, it cites to numerous instances in the specification to suggest that the inventors intended to invent only anti-IL-12 antibodies. It also notes that "[t]here is no description or support in the patents for antibodies that inhibit or affect . . . any cytokine other than IL-12." (*Id.*).

In its post-hearing brief, Abbott has agreed that the term "neutralizing antibody" is limited to antibodies that neutralize human IL-12. (Pl. Post-Hr'g Br. at 7) ("Without conceding the correctness of Centocor's position, Abbott is willing to agree for purposes of this case that, in the context of the claims of the '128 patent only, a 'neutralizing antibody' is an antibody that neutralizes IL-12."). However, it continues to reject Centocor's argument that the specification requires this construction. Instead, Abbott bases its concession on the arrangement of the term in the claims. "The term 'neutralizing antibody' by itself is not limited to neutralizing IL-12, but within the context of the claims, where that term is used in claims that require that the antibody bind to IL-12, the antibody neutralizes IL-12." (*Id.*).

Because this distinction bears on the construction of other disputed terms, further

discussion of the parties' reasoning is required. As noted above, proper claim construction adopts the perspective of one skilled in the relevant art at the time of the effective filing date of the application. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005). When construing a term, the Court should examine the "fully integrated written instrument," including *both* the claims themselves and the specification, unless the claims provide a "firm basis for construing the term." *Id.* at 1314-15.

Here, Abbott is incorrect that the claims, standing alone, support the proposed construction. Consider claim 7, which again is typical of how the term appears in the claims. Claim 7 depends upon claim 1, which modifies the word "antibody" by giving it the characteristic "binds to human IL-12." Claim 7 further modifies the word "antibody" by making it "neutralizing." According to the arrangement of the terms in the claims, both "neutralizing" and "binds to IL-12" separately modify the word "antibody." This arrangement suggests separate and independent characteristics of the antibody that may or may not overlap. Although Abbott's construction—that the antibody must "neutralize" IL-12— is one possible reading of the terms, other readings are plausible. As Centocor asserts, the claims could also be read to cover an antibody that binds to (but does not neutralize) IL-12 and neutralizes any other molecule.

This lack of clarity is further supported by the use of variants of the term "neutralizing" elsewhere in the claims. "Because claim terms are normally used consistently throughout the patent, the usage of a term in one claim can often illuminate the meaning of the same term in other claims." *Id.* at 1314. Claim 50, for example, reads as follows:

> 50. An isolated human antibody, or antigen-binding portion thereof that binds to human IL-12 and dissociates from human IL-12 with a K_d of l.34 x $l0^{-10}$ M or less, **and neutralizes human IL-12.**

‘128 Patent at col. 388 ll. 17-20 (emphasis added). This claim is structurally quite similar to the combination of claims 1 and 7, but the inventors elected to use the phrase “and neutralizes IL-12” instead of “wherein the antibody is a neutralizing antibody.” Although not dispositive, the patentees’ use of different language in similar claims at a minimum raises the question whether they intended “neutralizing antibody” to mean something different than “neutralizes IL-12.” *See Phillips*, 415 F.3d at 1314 (“Differences among claims can . . . be a useful guide in understanding the meaning of particular claim terms.”). *But see Curtiss-Wright Flow Control Corp. v. Velan, Inc.*, 438 F.3d 1374, 1380 (Fed. Cir. 2006) (“[T]wo claims with different terminology can define the exact same subject matter.”).

Thus, although the combination of claims 1 and 7 could plausibly yield Abbott’s construction, this is not a situation where “the use of a term within the claim provides a firm basis for construing the term.” *Phillips*, 415 F.3d at 1314. In *Phillips*, the Federal Circuit found a firm basis in the claim language for interpreting the term “ baffles.” *Id.* The court concluded that the use of “steel” to modify “baffles” strongly implied that “baffles” did not inherently mean objects made of steel. *Id.* Similarly, in *Mars, Inc. v. H.J. Heinz Co.*, 377 F.3d 1369 (Fed. Cir. 2004), the court interpreted the term “ingredients” in light of its position in the phrase “mixture of lipid and solid ingredients.” *Id.* at 1374. Because the parties agreed that “mixture” meant “a portion of matter consisting of two or more components,” the court determined that “ingredients” could not mean “starting materials” but must mean “components of a mixture after they have been combined.” *Id.* at 1373-76.

In these cases, the court found a “firm basis” in the claims because any other interpretation

of the disputed term would have led to a construction that was nonsensical or superfluous. *See also Voda v. Cordis Corp.*, 536 F.3d 1311, 1319 (Fed. Cir. 2008) (claims themselves did not provide firm basis for proposed meaning because they did not "inherently require" such meaning).[7] In contrast, the claims here—although certainly suggestive of the meaning that Abbott ascribes—do not by themselves provide for such a clear-cut interpretation. As mentioned, an equally plausible interpretation of "neutralizing" would cover any antibody that binds to IL-12 with the required level of affinity—whether or not it actually neutralizes IL-12—if it also binds to and neutralizes any other molecule—in other words, is a "neutralizing antibody." Such an antibody is not merely speculative. As described above, antibodies can bind to two or more antigens (i.e., have low specificity) but only neutralize one of them.[8]

As a result, the Court cannot follow Abbott's suggestion of adopting its proposed construction based on the claims alone. Rather, the Court must consult the specification and/or the prosecution history for clarification.[9]

2. "Inhibits [PHA] Blast Proliferation" and "Inhibits Human IFNγ production"

The parties next dispute the construction of the '128 patent terms "inhibits [PHA] blast

[7] For example, interpreting "baffles" in *Phillips* to include "made of steel" would render the presence of the word "steel" redundant. Similarly, interpreting "ingredients" to mean "starting components" would have yielded a nonsensical meaning akin to "combination of components that are not yet combined."

[8] An antibody that binds to IL-12 with the K_d and K_{off} rate required in claim 1 will not necessarily neutralize that antibody. As noted above, an antibody may have high affinity for an antigen but not neutralize it. In keeping with this, the specification and claims describe "affinity" and "neutralizing activity" as two separate characteristics. *See, e.g.*, '128 Patent at col. 46 ll. 7-8 ("To improve the activity (e.g., affinity or neutralizing activity) of an antibody . . .").

[9] Neither party has cited the prosecution history for support, and the Court assumes that it provides no guidance on this issue.

proliferation in an in vitro PHA assay"[10] and "inhibits human IFNγ production." Claims 8 and 13 are typical examples of how these terms appear in the claims:

> 8. The neutralizing antibody of claim 7, or an antigen-binding portion thereof, which **inhibits phytohemagglutinin blast proliferation in an in vitro PHA assay** with an IC_{50} of l x $l0^{-9}$ M or less. . . .
>
> 13. The neutralizing antibody of claim 7, or an antigen-binding portion thereof, which **inhibits human IFNγ production** with an IC_{50} of l x $l0^{-11}$ M or less.

'128 Patent at col. 385 ll. 36-39, 57-59 (emphasis added). The disputed terms refer to several example assays conducted by the inventors and disclosed in the specification. In those example assays, the inventors used IL-12 to stimulate proliferation and IFNγ production.

As with "neutralizing antibody," Centocor contends that the claims are unduly expansive. Because "proliferation" and "human IFNγ production," as written, do not require stimulation by IL-12, these processes "could be caused by any cytokine, not just IL-12" and "could have nothing to do with any effect of the antibody to IL-12." (Def. Reply Br. at 9) (emphasis omitted). Centocor asserts that this construction would extend the scope of the patent beyond the invention disclosed in the specification, which describes anti-IL-12 antibodies designed to counteract the activity of IL-12.

Abbott responds that the terms require no such construction and asks the Court to adopt the plain meaning of the terms as they appear in the claims.

As with "neutralizing antibody," however, the plain meaning of these terms is not clear based on the claim language alone. For example, claim 13 adds an additional characteristic to the

[10] The disputed term "inhibits phytohemagglutinin blast proliferation in an in vitro PHA assay" also appears in the claims as "inhibits phytohemagglutinin blast proliferation in an in vitro phytohemagglutinin blast proliferation assay (PHA assay)." The parties agree that these are synonymous.

"neutralizing" antibody that "binds to IL-12" described in claims 1 and 7. One fair reading of claim 13 is analogous to Abbott's proposed interpretation of "neutralizing antibody"—in other words, "within the context of the claims, where that term is used in claims that require that the antibody bind to IL-12, the antibody [inhibits human IFNγ production stimulated by IL-12]." (*See* Pl. Post-Hr'g Br. at 7). A second, equally fair reading is that the claims would cover any antibody that binds to and neutralizes IL-12 with the required level of affinity—whether or not it actually inhibits PHA blast proliferation stimulated by IL-12—if it also inhibits PHA blast proliferation stimulated by any other molecule. It is this second, broader reading that Abbott seeks to have the Court adopt here.

Because the claims do not provide a firm basis on which to construe the disputed terms, the Court must again look to other sources of intrinsic evidence.

3. Construing the Terms

"[C]laims must be construed so as to be consistent with the specification, of which they are a part." *Merck & Co. v. Teva Pharms., Inc.*, 347 F.3d 1367, 1371 (Fed. Cir. 2003); *see Phillips*, 415 F.3d at 1316 (citing *Merck* for this proposition).

When read in light of the specification, it is clear that the '128 patent claims should not be construed to encompass antibodies that neutralize and inhibit the activity of molecules other than IL-12. The specification makes evident that the patentees only intended to invent antibodies that bind to IL-12. The title of the patent is "Human Antibodies that Bind Human IL-12 and Methods for Producing." '128 Patent. The patent's "Summary of the Invention" section states that:

> The present invention provides human antibodies that bind human IL-12. The invention also relates to the treatment or prevention of acute or chronic diseases or conditions whose pathology involves IL-12, using the human anti-IL-12 antibodies of the invention.

Id. at col. 2 ll. 46-59. Identical or similar language is recited throughout the text. *See, e.g.*, *id.*, Abstract; *id.* at col. 30 ll. 60-61. The patent's "Detailed Description of the Invention" is entirely directed toward creation of an IL-12 antibody with particular preferred characteristics, including high specificity and affinity for IL-12.[11] Finally, with the exception of one subsection,[12] the ten examples in the specification exclusively describe testing, development, or studies of antibodies that bind to IL-12.[13]

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[11] Section 1 of the "Detailed Description of the Invention" is titled "Human Antibodies that Bind Human IL-12" and discloses only anti-IL-12 antibodies. *Id.* at col. 30 ll. 59; *see, e.g.*, *id.* at col. 31 ll. 1-31 (describing process of developing an antibody with high specificity and affinity for IL-12). The second part of the description describes a method for creating antibodies where "the antibody libraries . . . are preferably screened using recombinant human IL-12 as the antigen" in order to obtain "an anti-hIL-12 antibody of the invention." *Id.* at col. 40 ll. 14-17, 49-50.

The third, fourth, and fifth parts of the description appear to describe various methods for creating preferred antibodies, including at least one novel technique developed by the patentees. *See id.* at col. 45 ll. 64-67. These methods are described generically, and it is likely that the patentees believed these methods would be useful for creating antibodies other than anti-IL-12 antibodies. *See, e.g.*, *id.* at col. 45 ll. 61-67 ("Thus, for at least certain antibodies or antigens, phage display methods are limiting . . . . Accordingly, a method . . . was established to overcome this limitation and is provided by the invention."). However, this does not extend the scope of the patent beyond IL-12 antibodies because no other antibodies are described in the text. *See, e.g.*, *id.* at col. 48 ll. 14-25; col. 68 ll. 5-9. Methods, standing alone, are insufficient to extend the scope of a patent. *See In re Alonso*, 545 F.3d 1015, 1021-22 (Fed. Cir. 2008) (method for creating antibodies could not be a basis for claims to antibodies not separately described in invention).

The sixth and final part of the description describes various mechanisms and compositions for administering the antibodies of the invention to patients for treatment. Again, the only antibodies discussed in this section are IL-12 antibodies. *See* '128 Patent at col. 81 ll. 2-7, 34-67; col. 82 ll. 1-67.

[12] This subsection, titled "Binding to a Novel IL-12 Molecule," discusses a molecule comprising the same p40 subunit of IL-12 paired with a p19 subunit instead of a p35 subunit. *Id.* at col. 111 ll. 30-33. After briefly describing some features of the molecule, the section concludes that "[a]ntibodies which recognize p40 alone, but preferably in thecontext of a p70 molecule . . . are expected to also neutralize both the p35/p40 molecules and the p19/p40 molecules." *Id.* at col. 111 ll. 38-41. The paragraph makes clear that binding to this new molecule would be a beneficial, and apparently unanticipated, side use of antibodies that were developed to bind to and neutralize IL-12.

[13] *See id.* at col. 103 ll. 19-21 ("Example 1[:] Isolation of Anti-IL-12 Antibodies"); col. 108 ll. 37-41 ("Example 2[:] Mutation of Y61 [an IL-12 antibody] at Hypermutation and Contact Positions"); col. 109 ll. 30-33 ("Example 3[:] Functional Activity of Anti-hIL-12 Antibodies"); col. 113 ll. 57-59 ("Example 4[:] In vivo Activity of Anti-hIL-12 Antibodies"); col. 116 ll. 20-23 ("Example 5[:] Kinetic Analysis of Binding of Human Antibodies to Recombinant human IL-12"); col. 118 ll. 54-56 ("Example 6[:] Further Studies of J695 Affinity for IL-12"); col. 119 ll. 23-27 ("Example 7[:] Characteristics and Neutralization Activity of C17.15, a Rat

The inventors repeatedly state that one of the "preferred characteristics" of the invention's antibodies is the ability to neutralize IL-12. *See, e.g.*, *id.*, Abstract ("Preferred antibodies have high affinity for hIL-12 and neutralize hIL-12 activity . . ."); col. 10 ll. 31-33 ("In another aspect, the invention provides an isolated human antibody . . . that neutralizes the activity of human IL-12 . . ."); col. 30 ll. 62-63 ("Preferably, the human antibodies of the invention are recombinant, neutralizing human anti-hIL-12 antibodies."). Furthermore, every example in the specification of PHA blast proliferation and human IFNγ production uses IL-12 to stimulate those activities. *See id.* at col. 110 ll. 40-43; col. 111 ll. 16-19.

In light of the specification, it would be unduly overbroad to read the term "neutralizing antibody" as neutralizing *any* molecule. Instead, "neutralizing antibody" is more properly construed as "an antibody whose binding to human IL-12 results in inhibition of a biological activity of human IL-12." Similarly, it would be overbroad to construe "inhibits [PHA] blast proliferation" and "inhibits human IFNγ production" to refer to antibodies that inhibit *any* molecule capable of causing proliferation or IFNγ production. Instead, the claims are more properly construed as limited to PHA blast proliferation and human IFNγ production stimulated by IL-12.

Abbott contends that the Court's construction of the assay terms would improperly "read[] limitations from the specification into the claims." *Phillips*, 415 F.3d at 1323. The process of using IL-12 to stimulate PHA blasts appears only in the "Examples" section of the patent.

Monoclonal Antibody to Murine Interleukin-12"); col. 120 ll. 46-48 ("Example 8[:] Treatment of . . . Mice by . . . IL-12 Antibody Administration"); col. 123 ll. 24-26 ("Example 9[:] Clinical Pharmacology of J695 [an IL-12 antibody]"); col. 123 ll. 57-60 ("Example 10[:] Comparison of J695 [an IL-12 antibody] Produced by Two CHO Cell Lines").

Moreover, the inventors explicitly describe those examples as non-limiting and state that other assays known in the art can be used. *See* '128 Patent at col. 82 ll. 60-62; col 27 ll. 62-65. Abbott concludes that, because the patentees made clear that the examples were not intended to limit the scope of the invention, the Court should not require PHA blast proliferation and IFNγ production to be stimulated by IL-12. (Pl. Post-Hr'g Br. at 8) (citing *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1117 (Fed. Cir. 2004)).

These arguments are unavailing. It is true that some cases prior to *Phillips* held that "claims will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope 'using words or expression of manifest exclusion or restriction.'" *Innova,* 381 at 1117 (quoting *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004)). However, *Phillips* expressly discouraged this approach because it accorded too little weight to the specification:

> Assigning such a limited role to the specification, and in particular requiring that any definition of claim language in the specification be express, is inconsistent with our rulings that the specification is the single best guide to the meaning of a disputed term, and that the specification acts as a dictionary when it expressly defines terms used in the claims or when it defines terms by implication.

Phillips, 415 F.3d at 1320-21 (internal quotations omitted); *see also On Demand Mach. Corp. v. Ingram Indus.*, 442 F.3d 1331, 1340 (Fed. Cir. 2006) ("However, when the scope of the invention is clearly stated in the specification, and is described as the advantage and distinction of the invention, it is not necessary to disavow explicitly a different scope."). *Phillips* makes clear that the specification is the starting point for understanding a term, and such terms may be defined by implication as well as explicitly.

The Court's construction of the terms is consistent with the principles outlined in *Phillips*

and accords with other cases following that decision. *See Kinetic Concepts, Inc. v. Blue Sky Med. Grp., Inc.*, 554 F.3d 1010, 1018-19 (Fed. Cir. 2009) (limiting "wound" to skin wounds based on description in the specification); *Curtiss-Wright Flow Control Corp. v. Velan, Inc.*, 438 F.3d 1374, 1379 (Fed. Cir. 2006) (limiting "adjustable" to meaning consistent with specification); *On Demand*, 442 F.3d at 1340 (limiting "customer" to be consistent with the invention described in the specification). In *On Demand*, the Federal Circuit considered the construction of "customer" in the context of a patent for an on-demand book printing process. The patent described a process in which a "customer" could browse through a book selection at a computer terminal and order books, which would then be printed and bound on-site. *On Demand*, 442 F.3d at 1334. The patentee sought to prove infringement of a similar process that allowed retailers and publishers (but not the general public) to order books from a large-scale printer. *Id.* at 1335. Although the specification did not specifically limit "customer" to "retail customer," the Federal Circuit found that the specification, taken as a whole, clearly disclosed an invention directed to use by the ultimate consumer rather than wholesalers. *Id.* at 1339-40. Within this scope, the court held that "customer" could not have a broader meaning:

> In *Phillips*, the *en banc* court explained that the role of the specification is to describe and enable the invention. In turn, the claims cannot be of broader scope than the invention that is set forth in the specification. Although we agree with the district court that the Ross invention does not concern itself with whether the "customer" reads the book or obtains it for resale, the focus of the Ross patent is immediate single-copy printing and binding initiated by the customer and conducted at the customer's site. The district court's definition of "customer" cannot eliminate these constraints in order to embrace the remote large-scale production of books for publishers and retailers.

Id. (internal citations omitted). Here, although the terms "neutralizing antibody," "inhibits [PHA] blast proliferation," and "inhibits human IFNγ production" are not expressly limited to IL-12, they

cannot be interpreted to go beyond the scope of the invention that is set forth in the specification. That invention encompasses antibodies that bind to and neutralize IL-12. As in *On Demand*, the Court's definitions of these terms cannot eliminate the clear constraints of the patent in order to embrace antibodies that neutralize or inhibit any molecule.

Abbott's argument that the Court would be according undue weight to the examples also misses the mark. It is true that the Federal Circuit has consistently rejected the argument that a patent should be construed more narrowly based on examples in the specification. *Phillips*, 415 F.3d at 1323 ("[A]lthough the specification often describes very specific embodiments of the invention, we have repeatedly warned against confining the claims to those embodiments."); *see, e.g., Kara Tech. Inc. v. Stamps.com Inc.*, 582 F.3d 1341, 1347 (Fed. Cir. 2009) (rejecting construction of "security indicia" that required a key described in the specification examples); *Epistar Corp. v. Int'l Trade Comm'n*, 566 F.3d 1321, 1337 (Fed. Cir. 2009) (declining to limit thickness of "substrate" to thickness disclosed in a preferred embodiment); *Medegen MMS, Inc. v. ICU Med., Inc.*, 317 Fed. Appx. 982, 987 (Fed. Cir. 2008) (rejecting argument that "plug" should be limited to the plug described in the preferred embodiment); *Cohesive Techs., Inc. v. Waters Corp.*, 543 F.3d 1351, 1360 (Fed. Cir. 2008) (declining to limit "rigid" to monomeric particles even though embodiments used only monomeric particles).

Although examples are not limiting, they are not irrelevant; they help to disclose what has actually been invented, and what the inventors intended to claim. "Ultimately, the interpretation to be given a term can only be determined and confirmed with a full understanding of what the inventors actually invented and intended to envelop with the claim. The construction that stays true to the claim language and most naturally aligns with the patent's description of the invention

will be, in the end, the correct construction." *Phillips*, 415 F.3d at 1316 (citing *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998)).

Accordingly, the Court will adopt Centocor's proposed constructions of these terms:

CLAIM TERM	CONSTRUCTION
"neutralizing antibody" (claims 7-15, 29-40)	"an antibody whose binding to human IL-12 results in inhibition of a biological activity of human IL-12"
"inhibits [PHA] blast proliferation in an in vitro PHA assay" (claims 8-12, 33-37, 55-57)	"inhibits the proliferation of human PHA blasts stimulated by IL-12"
"inhibits human IFNγ production" (claims 13-15, 38-40, 58-60)	"inhibits human IFNγ production[14] stimulated by IL-12"

B. Limiting the Claim Terms of the '485 Patent to the P40 Subunit

The parties appear to have a similar dispute concerning terms in the '485 patent.[15] The proposed constructions of the disputed terms are as follows:

[14] The Court declines to adopt Centocor's proposed wording "inhibits the production of human interferon-γ" because that aspect of the term is clear as written and requires no construction.

[15] These constructions were explicitly raised for the first time by Centocor in its supplemental claim construction brief after the *Markman* hearing. (*See* Def. Post-Hr'g Br. at 2-5). Although the Court will address these arguments here, such an approach to a claim construction hearing is to be discouraged.

CLAIM TERM	ABBOTT'S PROPOSED CONSTRUCTION	CENTOCOR'S PROPOSED CONSTRUCTION
"neutralizes" (claim 25)	"an antibody whose binding to an antigen results in inhibition of a biological activity"	"neutralizes a biological activity of the interleukin **to which the antibody is bound**"
"inhibits [PHA] blast proliferation in an in vitro PHA assay" (claims 10, 26)	"inhibits the proliferation of stimulated human PHA blasts"	"inhibits the proliferation of human PHA blasts **stimulated by the interleukin to which the antibody is bound**"
"inhibits human IFNγ production" (claims 10, 26)	plain meaning	"inhibits the production of human interferon-γ **stimulated by the interleukin to which to antibody is bound**"

(Gunther Decl. Exs. 8, 9; Def. Post-Hr'g Br. at 2-5) (emphasis added).

As an initial matter, the Court notes that the '485 patent claims a broader invention than the '128 patent. The '128 patent is explicitly limited to IL-12 antibodies by the plain language of claims 1, 29, and 50. *See, e.g.*, '128 Patent at col. 385 ll. 11-15 ("An isolated human antibody . . . that binds to human IL-12 . . ."). The '485 patent, on the other hand, seeks to claim antibodies that bind to the p40 subunit found in IL-12, even where that subunit appears in other molecules. *See, e.g.*, U.S. Patent No. 7,504,485 at col. 381 ll. 54-61 (filed Mar. 25, 1999) ("[An] antibody . . . [that] is capable of binding to . . . the p40 subunit of IL-12 and a p19 subunit."). Both patents, however, use the same specification.[16]

[16] The broader claims of the '485 patent appear to be supported by the inventors' disclosure that some antibodies of the invention inhibit IL-12 by binding to its p40 subunit. *See, e.g., id.* at col. 59 ll. 50-52 ("recognizing p40 epitope preferably in the context of the p70 p40/p35 heterodimer" disclosed as a preferred characteristic); col. 60 ll. 65-67 (same); col. 62 ll. 19-22 (same); col. 101 ll. 14-15, 26-27, 30-31 (example using p40 to screen for desired antibodies). In addition, a subsection in the examples refers to an interleukin comprising a p40 and a p19 subunit that the antibodies of the invention "are expected to also neutralize." *Id.* at col. 113 ll. 54-56. Whether these disclosures are sufficient to support the '485 patent's broader scope is a question of validity for another day.

Aside from slight variation based on the broader scope of the '485 patent, the parties' positions here are identical to their positions with regard to the '128 patent. The core disagreement is whether the terms should be interpreted as limited to interleukins comprising a p40 subunit. Abbott contends that the claim language of the patents is sufficiently clear on its face, even where that language is not explicitly limited to processes or characteristics related to interleukins comprising a p40 subunit. Centocor contends that the specification teaches only how to make antibodies that bind to the p40 subunit of IL-12 and that the claim terms of the '485 patent should not be construed more broadly.[17]

1. "Neutralizes"

Although the '485 patent has a broader scope than the '128 patent, the reasoning discussed above applies here with equal force. The term "neutralizes" appears in the following chain of independent and dependent clauses:

> 15. A pharmaceutical composition comprising an isolated human antibody, or antigen-binding portion thereof, **which is capable of binding to an interleukin comprising a p40 subunit**, and further comprising an additional agent. . .
>
> 25. The composition of claim 15, wherein the antibody, or antigen-binding portion thereof, **neutralizes** a biological activity of the interleukin.

Id. at col. 382 ll. 64-67; col. 383 ll. 26-28 (emphasis added). Centocor contends that, as written, the phrase "neutralizes a biological activity of the interleukin" is ambiguous and could refer to an interleukin other than "the interleukin comprising a p40 subunit" described in claim 15. Abbott appears to maintain that no construction is necessary.

At the outset, the Court notes that the use of "neutralizes" here is much clearer than the

[17] The parties also dispute the addition of "PHA blasts" to the construction of "inhibits human IFNγ production." This aspect of the dispute is discussed in a following section.

use of "neutralizing antibody" in the '128 patent. In particular, the use of the definite article "the" to refer to "interleukin" strongly suggests that "the interleukin" in claim 25 is the "interleukin comprising a p40 subunit" introduced in claim 15. However, insofar as any ambiguity exists, Centocor is correct that claim 25 must be construed as neutralizing a biological activity of the interleukin to which the antibody is bound—in other words, the interleukin comprising a p40 subunit discussed in claim 15.

Accordingly, the Court adopts the following construction of "neutralizes" in claim 25: "The composition of claim 15, wherein the antibody . . . neutralizes a biological activity of the interleukin comprising a p40 subunit."

2. "Inhibits [PHA] Blast Proliferation" and "Inhibits Human IFNγ production"

The same reasoning also holds true for the assay-related claim terms, which appear in claims 10 and 26 of the '485 patent. Because the context is slightly different, the Court will address these claims separately, beginning with claim 26. The terms appear in claim 26 as follows:

> 26. The composition of claim 25, wherein the antibody, or antigen binding portion thereof, **inhibits phytohemagglutinin blast proliferation in an in vitro PHA assay** with an IC_{50} of l x $l0^{-9}$ M or less, or which **inhibits human IFNγ production** with an IC_{50} of l x $l0^{-10}$ M or less.

Id. at col. 383 ll. 29-33 (emphasis added). By reference to claim 25 (see above), claim 26 further describes an antibody that binds to and neutralizes an interleukin comprising a p40 subunit. When read in conjunction with the specification, which only discloses antibodies that bind to the p40 subunit of IL-12, claim 26 would exceed the scope of the invention if it covered antibodies that inhibited proliferation or IFNγ production stimulated by *any* molecule. Were it otherwise, the cell proliferation and IFNγ production in the assays could be caused by any cytokine, not just one

comprising a p40 subunit, even though no other cytokine is described by the patent. (*See* Def. Reply Br. at 9). Therefore, the proper construction limits these terms to proliferation and IFNγ production stimulated by an interleukin comprising a p40 subunit.

Accordingly, the Court will adopt the following construction as to claim 26: "inhibits the proliferation of human PHA blasts stimulated by the interleukin comprising a p40 subunit" and "inhibits human IFNγ production stimulated by the interleukin comprising a p40 subunit."

The assay-related claim terms also appear in claim 10. The chain of independent and dependent claims that includes claim 10 is as follows:

> 1. A pharmaceutical composition comprising an isolated human antibody, or antigen-binding portion thereof, **which is capable of binding to an epitope of the p40 subunit of IL-12**, and further comprising an additional agent. . . .
>
> 6. The composition of claim 1, wherein the antibody, or antigen-binding portion thereof, is **further capable of binding to** a first heterodimer and is also capable of binding to a second heterodimer, wherein the first heterodimer comprises **the p40 subunit of IL-12 and the p35 subunit of IL-12**, and wherein the second heterodimer comprises **the p40 subunit of IL-12 and a p19 subunit**.
>
> 7. The composition of claim 6, wherein the antibody, or antigen-binding portion thereof, neutralizes a biological activity of the first heterodimer. . . .
>
> 9. The composition of claim 6, wherein the antibody, or antigen-binding portion thereof, neutralizes a biological activity of the first heterodimer and the second heterodimer.
>
> 10. The composition of claims 7 or 9, wherein the antibody, or antigen binding portion thereof, **inhibits phytohemagglutinin blast proliferation in an in vitro PHA assay** with an IC_{50} of l x $l0^{-9}$ M or less, or which **inhibits human IFNγ production** with an IC_{50} of l x $l0^{-10}$ M or less.

'485 Patent at col. 381 ll. 33-36, 54-60, 62-64; col. 382 ll. 32-39 (emphasis added). Unlike claim 26, the antecedent terms here do not refer to an interleukin comprising p40. Rather, they define a "first heterodimer" comprising p40 and p35 and a "second heterodimer" comprising p40 and p19.

For the reasons discussed above, where the "antibody" referred to by the assays is one that can bind to both p40/p35 and p40/p19, the proliferation and IFNγ production in claim 10 must be construed as stimulated by either p40/p35 or p40/p19.

Accordingly, the Court will adopt the following construction of the assay-related terms in claim 10: "inhibits "inhibits the proliferation of human PHA blasts stimulated by the heterodimer comprising the p40 subunit of IL-12 and the p35 subunit of IL-12 or the heterodimer comprising the p40 subunit of IL-12 and a p19 subunit" and "inhibits human IFNγ production stimulated by the heterodimer comprising the p40 subunit of IL-12 and the p35 subunit of IL-12 or the heterodimer comprising the p40 subunit of IL-12 and a p19 subunit."[18]

CLAIM TERM	**CONSTRUCTION**
"neutralizes" (claim 25)	"neutralizes a biological activity of the interleukin comprising a p40 subunit"
"inhibits [PHA] blast proliferation in an in vitro PHA assay" (claims 10, 26)	"inhibits the proliferation of human PHA blasts stimulated by a heterodimer comprising the p40 subunit of IL-12 and the p35 subunit of IL-12 or a heterodimer comprising the p40 subunit of IL-12 and a p19 subunit"
"inhibits human IFNγ production" (claims 10, 26)	"inhibits human IFNγ production stimulated by a heterodimer comprising the p40 subunit of IL-12 and the p35 subunit of IL-12 or a heterodimer comprising the p40 subunit of IL-12 and a p19 subunit"

C. Limiting the Claim Terms of the '128 and '485 Patents to PHA Blasts

The parties next dispute whether two of the assays referred to in the claims of both patents should be limited to experiments involving PHA blasts. The disputed terms and the parties' proposed constructions are as follows:

[18] Centocor proposes a common construction for all three terms using the phrase "to which the antibody is bound," with slight variations. Although this construction is shorter and simpler, the Court declines to adopt it in favor of a more precise construction.

CLAIM TERM	ABBOTT'S PROPOSED CONSTRUCTION	CENTOCOR'S PROPOSED CONSTRUCTION
"inhibits IL-12 binding to its receptor in an IL-12 receptor binding assay (RBA)" ('128 Patent claims 61-63)	plain meaning	"inhibits IL-12 binding to IL-12 receptors **on human PHA blasts**"
"inhibits human IFNγ production" ('128 Patent claims 13-15, 38-40, and 58-60; '485 patent claims 10, 26)	plain meaning	"inhibits the production of human IFNγ **by human PHA blasts**"

(Pl. Post-Hr'g Br. at 7; Def. Opening Br. at 12-13) (emphasis added). In support of its proposed constructions, Centocor points out that the assays conducted by the patentees in the specification all used PHA blast cells. "No other cell[] types are used or even mentioned in the patents' description of . . . [the] biological assays. Thus, Centocor's construction reflects the teachings of the patent specifications by making it clear that the [assays are] performed with PHA blast cells." (Def. Op. Br. at 14). Abbott responds that Centocor's construction would improperly import limitations from the specification into the claims.

The Court returns, once again, to first principles. A correct claim construction should correspond to "the meaning that the term would have to a person of ordinary skill in the art in question at the time of . . . the effective filing date of the patent application.." *Phillips*, 415 F.3d at 1313. "[A]lthough the specification often describes very specific embodiments of the invention, we have repeatedly warned against confining the claims to those embodiments." *Id.* at 1323.

In the context of the specification and the claims, Centocor's proposed construction would clearly constitute an improper limitation on claim scope. As an initial matter, the Court notes that the patents are directed to antibodies that bind to IL-12 (as discussed at length above), and this

scope could reasonably include assays using any type of cell that can be stimulated by IL-12. Turning to the claims, the Court finds no mention of PHA blasts in relation to the disputed terms. *See, e.g.*, '128 Patent at col. 388 ll. 17-67; '485 Patent at col. 382 ll. 35-39. On the contrary, the claims specifically limit other types of assays to PHA blasts while failing to do so with the assays disputed here. *See, e.g.*, '485 Patent at col. 382 ll. 35-39 ("inhibits [PHA] proliferation in an in vitro PHA assay").

Turning to the specification, the inventors provide several indications that they did not see PHA blasts as an essential requirement of the claimed assays. The assays using PHA blasts to test IL-12 receptor binding and IFNγ production appear exclusively in the "Examples" section of the patent. The specification further states that these examples "should not be construed as limiting in any way." '128 Patent at col. 82 ll. 60-62.[19] Finally, the specification states that "these indicators of hIL-12 biological activity can be assessed by one or more of several standard in vitro or in vivo assays known in the art . . ." *Id.* at col 27 ll. 62-65. Together, these aspects of the specification reveal an intent to encompass antibodies tested for IL-12 efficacy using any standard assays known in the art at the time of the invention, whether or not they are provided in the examples.

This interpretation is also supported by extrinsic evidence. At least one publication prior to the filing date disclosed a means of testing IL-12's ability to inhibit IFNγ production in cells other than PHA blasts. (*See* Gunther Decl. Ex. 7). Similarly, at least one pre-filing publication discloses an IL-12 receptor-binding assay that did not use PHA blast cells. (*See* Gunther Decl. Ex. 7). Where the patents clearly encompass antibodies that bind to IL-12, and where several assays

[19] Because the specifications in the '485 and the '128 patents are identical, citations are given to the '128 patent only.

existed for testing such binding, the disputed claims should not be limited to assays involving PHA blasts.

Accordingly, the Court will adopt Abbott's proposal that the terms need no construction in this regard.

D. Limiting "Additional Agent" to Exclude "Pharmaceutically Acceptable Carriers"

Next, the parties dispute whether the prosecution history should limit the meaning of "additional agent" as it appears in claims 1 and 15 of the '485 patent. The disputed term and the parties' proposed constructions are as follows:

CLAIM TERM	ABBOTT'S PROPOSED CONSTRUCTION	CENTOCOR'S PROPOSED CONSTRUCTION
"additional agent" (claims 1, 15)	plain meaning	"an agent **other than a pharmaceutically acceptable carrier** which imparts a beneficial attribute to the therapeutic composition"

(Pl. Post-Hr'g Br. at 1; Def. Opening Br. at 14) (emphasis added). The parties agree that "additional agent," as defined by the specification, would include pharmaceutically acceptable carriers. (*See* Def. Op. Br. at 15; Pl. Op. Br. at 20). However, Centocor contends that Abbott disclaimed coverage for pharmaceutically acceptable carriers during the prosecution of the '485 patent.

The Court briefly describes the relevant history. While the '485 patent was being prosecuted, the PTO declared an interference between the '128 patent and Centocor's pending '994 application. The interference involved three claims in the Centocor application and a number

of claims in the '128 patent, including claim 64.

At the same time, the examiner advised Abbott that some claims in its '485 patent application were not allowable because they interfered with the same '994 application claims. (*See* Def. Opening Br. Ex. 9). Claim 142 of Abbott's patent application (which became issued '485 claim 1) was among the disallowed claims. Thus, both claim 64 of the '128 patent and claim 142 of the '485 patent application[20] were deemed to interfere with three claims of Centocor's '994 application:

'128 patent, claim 64	64. A pharmaceutical composition comprising an antibody or an antigen binding portion thereof of claims 1, 16, 21, 27, 29, 41, 44, 45, 48, 50, 51, **and a pharmaceutically acceptable carrier.**
'485 patent application, claim 142	142. An isolated human antibody, or antigen-binding portion thereof, which is capable of binding to an epitope of the p40 subunit of IL-12.

[20] The '485 patent only received that number on approval. For the purposes of this order, however, the Court will use "'485 patent application" to refer to the application that ultimately gave rise to the '485 patent.

'994 application claims corresponding to the interference count	1. An isolated human antibody, or an antigen-binding portion thereof, that binds to human IL-12, wherein said human antibody is a neutralizing antibody**.** 102. An isolated human antibody, or antigen-binding portion thereof that binds to human IL-12 and disassociates from human IL-12 with a K_d of 1 x 10^{-10} M or less, as determined by surface plasmon resonance. 103. An isolated human antibody, or an antigen-binding portion thereof, which disassociates from human IL-12 with a K_d of 1 x 10^{-10} M or less and binds to an epitope on the p40 subunit of human IL-12.

(Pl. Reply Br. at 9). In response, Abbott amended a number of claims of the '485 application, including claim 142. That claim was amended as follows:

> 142. ~~An~~ A pharmaceutical composition comprising an isolated human antibody, or antigen-binding portion thereof, which is capable of binding to an epitope of the p40 subunit of IL-12 **and an additional agent**.

(*Id.*) (emphasis added). The '485 patent was thereafter approved.

Centocor asserts that Abbott added "additional agent" to claim 142 to distinguish it from claim 64 of the '128 patent. Because claim 64 pairs an antibody and "a pharmaceutically acceptable carrier" and claim 142 pairs an antibody and "an additional agent," Centocor contends that the only way they can be distinct is if "additional agent" excludes pharmaceutically acceptable carriers.

In response, Abbott asserts that it would be improper to read an exclusion into the '485 patent based on language in the '128 patent. Instead, the only proper comparison is between the '485 patent application and the '994 application. Because the '994 application did not claim a

"pharmaceutically acceptable carrier" and an antibody, "additional agent" cannot be said to exclude that term. Abbott also contends that, in any case, the supposed disavowal of pharmaceutically acceptable carriers is too unclear and ambiguous as a matter of law to justify Centocor's proposed construction.

"[W]here the patentee has unequivocally disavowed a certain meaning to obtain his patent, the doctrine of prosecution disclaimer attaches and narrows the ordinary meaning of the claim congruent with the scope of the surrender." *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1324 (Fed. Cir. 2003). However, the bar for such disclaimer is high. "[B]ecause the prosecution history represents an ongoing negotiation between the PTO and the applicant, . . . it often lacks the clarity of the specification . . ." *Phillips*, 415 F.3d at 1317. Therefore, "in order to disavow claim scope during prosecution a patent applicant must clearly and unambiguously express surrender of subject matter." *Voda*, 536 F.3d at 1321 (internal quotations omitted); *Sorensen v. Int'l Trade Comm'n*, 427 F.3d 1375, 1378-79 (Fed. Cir. 2005); *see also Omega Eng'g*, 334 F.3d at 1324 ("We have . . . declined to apply the doctrine of prosecution disclaimer where the alleged disavowal of claim scope is ambiguous."); *DeMarini Sports v. Worth, Inc.*, 239 F.3d 1314, 1326-27 (Fed. Cir. 2001) (patentee's silence was insufficient to construe claim term).

Under this standard, Abbott's modification of claim 142 to include "additional agent" is not so clear and unambiguous as to constitute a disavowal of claim scope. First, Abbott never clearly stated that the amendment was meant to distinguish claim 142 from claim 64. On the contrary, the evidence indicates that Abbott borrowed "additional agent" from claim 175 of the '485 patent application, and that it borrowed this language because the examiner said claim 175 did not interfere with the '994 application. (*See* Def. Opening Br. Ex. 8 at 16, 16 n.2) ("[T]he

[interfering] independent claims have been amended to include the subject matter of the dependent claims that have been indicated by the Examiner as not interfering with the claims of the '994 application. For example, claim 142 has been amended to incorporate the subject matter of claim 175 [of the '485 application].''). Thus, nothing in the prosecution history indicates that either the examiner or the patentees ever looked to the '128 patent as a justification for including the term "additional agent."

Centocor points to case law suggesting that an amendment can itself constitute a clear and unambiguous disavowal of claim scope. *See Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1327 (Fed. Cir. 2003) ("[T]he prosecution history may not be used to infer the intentional narrowing of a claim absent the applicant's clear disavowal of claim coverage, such as an amendment to overcome a rejection."); *York Prods. v. Central Tractor Farm & Family Ctr.*, 99 F.3d 1568, 1575 (Fed. Cir. 1996) ("Unless altering claim language to escape an examiner rejection, a patent applicant only limits claims during prosecution by clearly disavowing claim coverage."); *Lemelson v. General Mills, Inc.* 968 F.2d 1202, 1207-08 (Fed. Cir. 1992) ("Lemelson cannot acquiesce to a rejection and to an agreed alternative, and now years later shift his stance 180 degrees to argue for a second bite at the abandoned apple."). This is true as a general principle, but unavailing in this context. Examining claim 142 in light of the prosecution history only suggests that the inventors surrendered the broader "isolated antibody" in favor of the narrower "isolated antibody . . . and an additional agent." Reading a surrender of "pharmaceutically acceptable carrier" into the amendment requires a wholly different inference not supported by the record.

In the absence of any clear reference by the examiner or the applicant to claim 64, Centocor

essentially asks the Court to engage in tea-leaf reading. This the Court cannot do. *DeMarini Sports, Inc. v. Worth, Inc.*, 239 F.3d 1314 (Fed. Cir. 2001), is instructive. In *DeMarini*, the Federal Circuit considered the meaning of "frame" in the context of a patent for a softball bat. Appellant contended that, had it held any other construction of "frame" than the one it proposed, it would have used that alternate construction during prosecution to distinguish its invention from prior art. The Federal Circuit rejected this argument as too ambiguous. "[W]e can draw no inference from what DeMarini did not argue. It could just as easily be presumed from DeMarini's silence that DeMarini [intended a different definition of the term than the one it proposes on claim construction]." *Id.* at 1326-27. Here, as in *DeMarini*, the ambiguity about the reasons for amending claim 142 could lead to any number of reasonable conclusions. *Id.*; *see also Golight, Inc. v. Wal-Mart Stores, Inc.*, 355 F3d 1332 (Fed. Cir. 2004) ("Because the statements in the prosecution history are subject to multiple reasonable interpretations, they do not constitute a clear and unmistakable departure . . ."). To conclude that the amendment was meant to distinguish between "additional agent" and "pharmaceutically acceptable carrier" would be going too far on the evidence presented.

Accordingly, the Court will follow Abbott's suggestion that "additional agent" needs no construction.

E. "Human Antibody"

Finally, the parties dispute the meaning of "human antibody." Their proposed constructions of the disputed term are as follows:

CLAIM TERM	ABBOTT'S PROPOSED CONSTRUCTION	CENTOCOR'S PROPOSED CONSTRUCTION
"human antibody"	"an antibody that is derived from human DNA and not from the DNA of any non-human species"	"a human antibody includes antibodies having variable and constant regions corresponding to human germline immunoglobulin sequences as described by Kabat et al. (See Kabat, et al. (1991) Sequences of Proteins of Immunological Interest, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242), but the antibody can have up to twenty positions replaced with amino acid residues which are not part of the human germline immunoglobulin sequence"

(Def. Suppl. Br. at 13; Pl. Opp'n to Mot. to Amend Cl. Constr. at 18). The core disagreement concerns the effect of definitional language in the specification. Centocor interprets this language to expressly limit the meaning of "human antibody" in two ways, while Abbott asserts that the relevant text is exemplary and non-limiting.

Neither party argues that the claims themselves inform the meaning of the term, so the analysis begins with the language in the specification.[21] The specification expressly defines the disputed term as follows:

> **The term "human antibody" includes antibodies having variable and constant regions corresponding to human germline immunoglobulin sequences as described by Kabat et al. (See Kabat, et al. (1991) *Sequences of [P]roteins of Immunological Interest, Fifth Edition,* U.S. Department of Health and Human Services, NIH Publication No. 91-3242).** The human antibodies of the invention may include amino acid residues not encoded by human germline immunoglobulin sequences (e.g., mutations

[21] The disputed term appears in both the '128 and '485 patent claims. *See, e.g.*, '128 Patent at col. 386 ll. 16, 21, 26; '485 Patent at col. 382 ll. 45, 51, 58.

> introduced by random or site-specific mutagenesis in vitro or by somatic mutation in vivo), for example in the CDRs and in particular CDR3. The mutations preferably are introduced using the "selective mutagenesis approach" described herein. The human anti-body can have at least one position replaced with an amino acid residue, e.g., an activity enhancing amino acid residue which is not encoded by the human germline immunoglobulin sequence. **The human antibody can have up to twenty positions replaced with amino acid residues which are not part of the human germline immunoglobulin sequence.** In other embodiments, up to ten, up to five, up to three or up to two positions are replaced. In a preferred embodiment, these replacements are within the CDR regions as described in detail below. However, the term "human antibody," as used herein, is not intended to include antibodies in which CDR sequences derived from the germline of another mammalian species, such as a mouse, have been grafted onto human framework sequences.

'128 Patent at col. 26 ll. 55-67; col. 27 ll. 1-14 (emphasis added). Centocor's proposed definition focuses on the effect of the bolded type on the ultimate construction of the term. In its view, "the express definition of 'human antibody' limits the universe of antibodies that are covered by the term 'human antibody' to include those that correspond exactly to a Kabat germline sequence as well as those that have no more than twenty amino acid changes as compared to a germline sequence listed in Kabat." (Def. Mot. to Amend Cl. Constr. at 10).

The cited language does not support Centocor's construction. Centocor relies on the first sentence of the quoted text to limit "human antibody" to human germline sequences described in *Sequences of Proteins of Immunological Interest, Fifth Edition* ("Kabat"), a reference text published in 1991.[22] However, the Kabat citation in the specification follows the word "includes." Unless there is good reason to hold otherwise, this renders Kabat exemplary and non-limiting. "As a patent law term of art, 'includes' means 'comprising.' . . . Neither includes, nor comprising, forecloses additional elements that need not satisfy the stated claim limitations." *SanDisk Corp. v.*

[22] "Human germline sequences" are amino acid sequences that occur naturally within the human body. (*See* Def. Suppl. Br. at 2). Kabat listed germline amino acid sequences of human antibodies known at the time. (*See id.*).

Memorex Prods., Inc., 415 F.3d 1278, 1284 (Fed. Cir. 2005). Centocor appears to concede this, but suggests that the only additional antibodies falling within the definition are those having "up to twenty positions replaced with amino acid residues which are not part of the human germline immunoglobulin sequence."

Centocor's reading is strained. The better reading is that the first sentence is intended to encompass all antibodies taken directly from human germline sequences and known in the art at the time of filing, and that the Kabat citation is illustrative only. This reading makes more sense for several reasons. First, new human germline sequences were discovered between Kabat's publication in 1991 and the patent's filing in 1999. It would be highly unusual for an inventor to deliberately exclude from his or her invention eight years of development in the art. Second, it would make little practical sense to limit the scope of the patent to the sequences disclosed in Kabat, as the books used in 1991 had been replaced by 1999 with electronic databases that allowed for easier comparison of sequences. (*See* Pl. Opp'n to Mot. to Amend Cl. Constr. at 10-11). But most importantly, the specification repeatedly refers to human germline sequences listed in VBASE, a separate and regularly updated electronic database. *See, e.g.*, '128 Patent at col. 25 l. 58; col. 46 l. 6; col. 42 l. 1. It would make no sense for the definition to exclude explicitly a database relied upon by the inventors throughout the specification.

Abbott also asserts, and Centocor does not dispute, that several of the embodiments in the specification do not correspond to any of the sequences in Kabat. (Pl. Rebuttal Br. at 6-7).[23] Centocor's interpretation would therefore result in the exclusion of preferred embodiments, an

[23] The Court notes that Abbott's argument appeared in the last briefing filed on this issue. Nevertheless, Centocor could have sought leave to correct the record and did not do so.

outcome that is "rarely, if ever, correct." *Vitronics*, 90 F.3d at 1583; *Oatey Co. v. IPS Corp.*, 514 F.3d 1271, 1276-77 (Fed. Cir. 2008) (citing *Vitronics* for this proposition). Accordingly, the Court finds that the term "human antibody" is not limited to human germline sequences listed in Kabat.

Centocor's second argument concerns the statement in the text that "[t]he human antibody can have up to twenty positions replaced with amino acid residues which are not part of the human germline immunoglobulin sequence." As noted above, Centocor reads this language as placing an upper limit of twenty on the amount of genetic mutations that may be made to an antibody of the invention.

Again, this reading is strained and not supported by the language of the specification as a whole. First, the word "can" (as opposed to "must") is generally permissive and cuts against Centocor's interpretation. Second, as illustrated by the large block of non-bolded language above, Centocor's reading of this sentence effectively ignores a substantial part of the definitional text. When viewed in light of the entire definition, the "up to twenty" statement is more appropriately treated as an embodiment, rather than a hard limitation. Before the "up to twenty" statement is mentioned, the text states that "the human antibodies of the invention may include amino acid residues not encoded by human germline immunoglobulin sequences (e.g., mutations introduced by random or site-specific mutagenesis in vitro or by somatic mutation in vivo), for example in the CDRs and in particular CDR3." This clause broadly encompasses human germline sequences that have been altered or mutated in some way, of which an antibody with "up to twenty" mutations is a subset. The text goes on to state that the antibody "can have at least one position replaced," that it "can have up to twenty positions replaced" (the phrase at issue here), and that "in other

embodiments, up to ten, up to five, up to three, or up to two positions are replaced." If "can have up to twenty positions replaced" is mandatory, then the analogous, preceding language "can have at least one position replaced" should also be mandatory. But this is nonsensical, because the definition clearly encompasses antibodies that have had no positions replaced. The "at least one" statement must therefore be an embodiment, suggesting that the following "up to twenty" statement is also an embodiment. Furthermore, the sentence following the "up to twenty" statement uses the language "in *other* embodiments." (emphasis added). The term "other" suggests that preceding descriptions of the human antibody, including the "up to twenty" statement, were also intended to be embodiments. For these reasons, the text of the definition strongly suggests that the inventors did not intend "up to twenty" to be limiting.

Moreover, Abbott asserts, and Centocor does not dispute, that some of the antibodies described in the specification have more than twenty positions replaced with amino acid residues that are not part of the human germline sequence. (*See* Pl. Opp'n to Mot. to Amend Cl. Constr. at 11). Centocor's interpretation would therefore again result in the exclusion of preferred embodiments, an outcome that is highly likely to be incorrect.

Turning to the last sentence in the definitional text, the reader at last encounters explicit language of exclusion:

> However, the term "human antibody," as used herein, is not intended to include antibodies in which CDR sequences derived from the germline of another mammalian species, such as a mouse, have been grafted onto human framework sequences.

As this sentence makes clear, human antibody is defined in terms of derivation—it must have been derived from fully-human sequences, and antibodies that originated in other species are not encompassed by the invention.

Accordingly, the better construction of "human antibody" is one that explicitly limits the term to antibodies derived from human germline sequences, as Abbott proposes.[24] The Court will therefore adopt Abbott's proposed construction of "human antibody" as "an antibody that is derived from human DNA and not from the DNA of any non-human species."[25]

IV. Conclusion

For the foregoing reasons, the disputed claim terms are construed as follows:

1. the term "K_d" means "the dissociation constant of a particular antibody-antigen interaction";

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[24] This construction is also consistent with the rest of the specification. The concept of "human antibodies" is introduced very early in the patent. In the "Background of the Invention" section, the specification describes prior art "therapeutic strategies . . . designed to inhibit or counteract IL-12 activity," specifically IL-12-neutralizing antibodies. '128 Patent at col. 2 ll. 13–17. The strategies include fully-murine, chimeric, and humanized antibodies, in which "the variable regions of the antibody chains are murine-derived and the constant regions of the antibody chains are human-derived." *Id.* at col. 2 ll. 17-20, 34-40. These strategies are ineffective, the patent says, because these IL-12 antibodies elicit unwanted human immune responses. *Id.* at col. 2 ll. 25-30, 40-45. In light of these limitations, the specification describes the need for "an entirely human anti-IL-12 antibody." *Id.* at col. 2 ll. 48. Immediately after describing this need for an entirely human antibody, the specification summarizes its invention as one which provides "human antibodies that bind human IL-12." *Id.* at col. 2 ll. 55–56.

Furthermore, throughout the patent, the inventors underscore the desirability of keeping the antibodies of the invention as close to human germline sequence as possible. In fact, they explicitly define and recommend a process known as "backmutation" that is designed to keep the antibody as close to human germline sequence as possible without sacrificing affinity and neutralizing ability. *See, e.g.*, *id.* at col. 44 ll. 59-61 ("[I]t may be desirable to change these 60 amino acid differences back to the true germline sequences (i.e., 'backmutation' of framework residues to the germline configuration). Thus, the present invention can optionally include a backmutation step."). Given this, the inventors clearly believed that what made their antibodies "human" was that they were derived from human germlines rather than those of other mammals.

[25] Centocor's remaining arguments are easily dismissed. Relying upon the prosecution history, it contends that Abbott's expert adopted Centocor's proposed construction in testimony during a prior proceeding. (Def. Mot. to Amend Cl. Constr. at 10-11). When read in its entirety, however, the testimony clearly defines "human antibody" with reference to the derivation of the sequences, consistent with Abbott's construction. (*See* Pearson Decl. Ex. 12 ¶¶ 15-17) ("One of ordinary skill in the art as of March 1999 would appreciate the traditional scientific distinction between a non-human antibody sequence and a human antibody sequence *based on the species origin of the sequences*.") (emphasis added).

Centocor also appeals to extrinsic evidence. Given the clarity of the intrinsic evidence here, arguments based on extrinsic evidence lack utility and need not be considered. *See Phillips*, 415 F.3d at 1317 (extrinsic evidence is normally not dispositive, and it may be disregarded at the Court's discretion).

2. the term "K_{off}" means "the off rate constant for dissociation of an antibody from the antibody/antigen complex";

3. the term "surface plasmon resonance" means "an optical phenomenon that allows for the analysis of real-time biospecific interactions by detection of alterations in protein concentrations within a biosensor matrix";

4. the term "recombinant antibody" means "antibody that is prepared, expressed, created or isolated by recombinant means";

5. the term "pharmaceutically acceptable carrier" means "any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like that are physiologically compatible, including one or more of water, saline, sugars, alcohols, polyalcohols, wetting or emulsifying agents, preservatives, or buffers";

6. the term "neutralizing antibody" means "an antibody whose binding to human IL-12 results in inhibition of a biological activity of human IL-12";

7. the terms "inhibits phytohemagglutinin blast proliferation in an in vitro PHA assay" and "inhibits phytohemagglutinin blast proliferation in an in vitro phytohemagglutinin blast proliferation assay (PHA assay)," as they appear in the '128 patent, mean "inhibits the proliferation of human PHA blasts stimulated by IL-12";

8. the term "inhibits human IFNγ production," as it appears in the '128 patent, means "inhibits human IFNγ production stimulated by IL-12";

9. the term "neutralizes," as it appears in claim 25 of the '485 patent, means

"neutralizes a biological activity of the interleukin comprising a p40 subunit";

10. the term "inhibits phytohemagglutinin blast proliferation in an in vitro PHA assay," as it appears in claim 10 of the '485 patent, means "inhibits the proliferation of human PHA blasts stimulated by the heterodimer comprising the p40 subunit of IL-12 and the p35 subunit of IL-12 or the heterodimer comprising the p40 subunit of IL-12 and a p19 subunit";

11. the term "inhibits phytohemagglutinin blast proliferation in an in vitro PHA assay," as it appears in claim 26 of the '485 patent, means "inhibits the proliferation of human PHA blasts stimulated by the interleukin comprising a p40 subunit";

12. the term "inhibits human IFNγ production," as it appears in claim 10 of the '485 patent, means "inhibits human IFNγ production stimulated by the heterodimer comprising the p40 subunit of IL-12 and the p35 subunit of IL-12 or the heterodimer comprising the p40 subunit of IL-12 and a p19 subunit";

13. the term "inhibits human IFNγ production," as it appears in claim 26 of the '485 patent, means "inhibits human IFNγ production stimulated by the interleukin comprising a p40 subunit";

14. the term "inhibits IL-12 binding to its receptor in an IL-12 receptor binding assay (RBA)" needs no construction; and

15. the term "additional agent" needs no construction.

16. the term "human antibody" means "an antibody that is derived from human DNA and not from the DNA of any non-human species."

So Ordered.

/s/ F. Dennis Saylor
F. Dennis Saylor IV
United States District Judge

Dated: May 5, 2011